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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,302	09/14/2005	Kunihiro Ohta	07336.0009-00000	4635

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EXAMINER	
VOGEL, NANCY TREPTOW	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
06/22/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,302	OHTA ET AL.	
	Examiner	Art Unit	
	NANCY VOGEL	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-27* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-13 and 15-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/17/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 4- 27 are pending in the case. Claim 14 is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 7, 12-15, 17, 25, 26, 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Chauhan et al. (Gene 120, 1992, 281-286) (cited by applicants).

Chauhan et al. disclose a vector comprising a vector comprising a gene and a DNA sequence and a promoter for controlling transcription of the gene, wherein the order is the DNA sequence, the transcription promoter 3' to the DNA sequence, and the gene 3' to the transcription promoter, wherein the DNA sequence has 60% or greater sequence identity to the gene (see Fig. 1, vector pSSC-9). The reference discloses a method comprising inserting said vector into a cell (see abstract, page 283). Homologous recombination would occur between the homologous DNA sequences. It is noted that any recombinant gene is encompassed by the claims 13 and 14.

Applicants have argued that Chauhan does not anticipate the claims since in the vector disclosed, each of the genes is controlled by its own tk promoter, and the neor gene is flanked by restriction sites, and that the sequences flanking the neor gene that undergo homologous recombination are not under the control of a promoter, and

therefore the use of the pSSC-9 vector does not induce homologous recombination of a gene that is 3' to a promoter controlling transcription of the gene. However, it is maintained that Chauhan disclose the structural elements that are present in the claims, and therefore recombination would occur and does occur according to the method when the DNA is used in a system in which homologous recombination is occurring. Therefore, applicant's arguments are not found convincing.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 7, 12-15, 17, 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nickoloff et al. (Mol. Cell. Biol. 1992, 12, 12, 5311-5318) (previously cited).

Nickoloff et al. disclose a method for inducing homologous recombination of mammalian cells, wherein the efficiency of the homologous recombination of a neo gene for example, which has been embedded in the chromosome of a mammalian cell such as CHO cell, and regulated by a DEX reactive MMTV promoter, and a different neo gene or the like is enhanced by activating transcription form the aforementioned DEX-reactive MMTV promoter. The reference discloses embodiments in which the order of the elements is DNA sequence comprising the promoter MMTV, the neo' gene sequence, followed by a neo encoding gene (see Fig. 1, 5). The reference discloses that transcription enhances recombination between direct and inverted repeats and requires transcriptional activity in only one repeat, and when both repeats are transcriptionally active. Therefore, it would have been obvious to one of ordinary skill in the art that transcription.(i.e. placement of an active promoter at the 5' region) of either repeat would be encompassed. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicants have argued that it is not obvious to modify NIckoloff by moving the MMTV promoter to regulate the downstream neo gene. However, it is maintained that Nicoloff et al. discloses the known effect of increased homologous recombination between a genetic element when transcription of said genetic element is activated.

Therefore, the particular placement of the genetic element of interest, promoter, and genetic element with which homologous recombination is desired, would have been obvious to one of ordinary skill in the art. Applicants arguments that they obtain higher levels of transcriptional induction are not found convincing since no side by side comparison is performed, and since the data is not commensurate in scope with the claims.

Claims 2, 8, 18, 23 rejected under 35 U.S.C. 103(a) as being unpatentable over Nickoloff et al. as applied to claims 1, 5, 7, 12-15, 17, 25-27 above, and further in view of Lahti et al.,(Methods, 1999, 17, 4, 305-312) (cited by applicants).

Nickoloff et al. is cited for the reasons set forth above. The difference between the reference and the instant claims is that a particular cell line, which is DT40, are used, and a tetracycline inducible promoter is used. However, Lahti et al. disclose DT40 cells and disclose that said cells have higher rates of homologous recombination than other cell types, and disclose transcription of genes therein by means of a tetracycline-reactive promoter (see page 305). It would have been obvious to have used a cell type such as DT40 which has increased levels of homologous recombination, in the method disclosed by Nickoloff et al. in order to obtain said higher levels of recombination. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicants arguments regarding Nickoloff have been maintained for this rejection, and therefore for the reasons set forth above the rejection is maintained.

Claims 9, 10, 19, 20, rejected under 35 U.S.C. 103(a) as being unpatentable over Nickoloff et al. as applied to claims 1, 5, 7, 12-15, 17, 25-27 above, and further in view of Slebos, (Biochem. Biophys. Res. Comm. 2001, 281, 1, 212-219) (cited by applicants).

Nickoloff et al. is cited for the reasons set forth above. The difference between the reference and the instant claims is that the gene and DNA sequence are those encoding EGFP or EBFP. However, Slebos et al. discloses the EBFP and EGFP genes and their introduction into a mammalian cell such as a DT-40 cell, in a method of homologous recombination (see abstract, see 214-215). IT would have been obvious to have used easily assayable genes, such as EGFP or EBFP as disclosed by Slebos, in a method of recombination and in a vector and cell used for said method, in order to more easily measure and assay results. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicants arguments regarding Nickoloff have been maintained for this rejection, and therefore for the reasons set forth above the rejection is maintained

Claims 4, 6, 11, 16, 21, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nickoloff as applied to claims 1, 5, 7, 12-15, 17, 25- 27 above, and further in view of Phi-van (Biochemistry 1996, 35, 10735-10742) or Israel et al. (Nuc. Acids. Res., 17, 12, 1989, 4589-4604) (both cited by applicants).

Nickoloff et al. is cited for the reasons set forth above. The difference between the claims and the references is that an MAR, which may be from the chicken lysozyme

gene, and/or an enhancer, may be present. However, Phi-van et al. disclose the MAR in the vicinity of the chicken lysozyme gene, and discloses a method for enhancing the expression of structural genes that are in the vicinity of the expression unit (see Fig. 1, Table 1). Israel et la. disclose an MMTV enhancer region, which is present in the vicinity of the MMTV promoter. IT would have been obvious to one of ordinary skill in the art to have included known elements, such as MAR and or enhancer regions, in the construct and method of Nicoloff et al. since such elements were known and disclosed to aid in transcriptional activity. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicants arguments regarding Nickoloff have been maintained for this rejection, and therefore for the reasons set forth above the rejection is maintained

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nickoloff in view of Phi-van (Biochemistry 1996, 35, 10735-10742) or Israel et al. (Nuc. Acids. Res., 17, 12, 1989, 4589-4604)as applied to claims 1, 4-7, 11-17, 25-27 above, and further in view of (Lahti et al., Methods, 1999, 17, 4, 305-312) (cited by applicants).

Nickoloff et al., Phi-van, Israel et al. are cited for the reasons set forth above. The difference between the references and the instant claims is that a particular cell line, which is DT40, are used. However, Lahti et al. disclose DT40 cells and disclose that said cells have higher rates of homologous recombination than other cell types (see 305). It would have been obvious to have used a cell type such as DT40 which has

increased levels of homologous recombination, in the method disclosed by Nickoloff et al. in view of Phi-van and Israel, in order to obtain said higher levels of recombination. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicants arguments regarding Nickoloff have been maintained for this rejection, and therefore for the reasons set forth above the rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
6/21/10